REMARKS

Applicant wishes to thank Examiner Scheiner for the courtesy extended to the representative, Nancy Vensko, attorney of record, on May 19, 2004. The Interview Summary Form PTOL-413 summarizes the discussions held at the personal interview. The present response to the outstanding Office Action includes the substance of the Examiner Interview.

A. Disposition of Application

Claims 3-6, 9-13, and 23, 25, and 26 are pending in the application. Claims 1, 2, 7, 8, 14-22, and 24 have been canceled, and Claims 3, 5, 6, 9, 23, 25, and 26 have been amended, both in order to cancel or excise non-elected subject matter, and thus for reasons unrelated to patentability. The Specification has been amended to include a claim to priority. An Abstract has been added to the Specification. No new matter is being added herewith.

B. Compliance with 35 USC 102(a)

The Patent Office rejected Claims 1-6, 9-13, and 22-26 under 35 USC 102(a) as being anticipated by Xu et al., Nature Med. 4: 37-42 (Jan 1998). The claims must be patentable over the prior art. Xu et al., however, does not constitute prior art date-wise. This is because the application claims the benefit of priority of U.S. Provisional Application No. 60/068,655 filed 23 December 1997. (The Specification has been amended to include a claim to priority.) Attached is a copy of the priority application itself obtained from the U.S. Patent Office. Additionally attached is a copy of the Declaration by inventors claiming the benefit of priority. Based on the claim to priority, the rejection under 35 USC 102(a) over Xu et al. should be withdrawn.

C. Compliance with 35 USC 112/1

The Patent Office rejected Claims 1-3, 5, 6, 9-11, 13, and 22-26 under 35 USC 112/1 as being drawn to subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. According to MPEP 2163 IIA3(a)(ii) describing a written description for a claim drawn to a genus (an expression vector) as opposed to a species (CMV expression vector), the written description requirement for a claimed genus may be satisfied

through sufficient description of a representative number of species. "Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species." Similarly, here, description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus (an expression vector) embraces. Here, in the molecular biology arts, applicant disclosed CMV expression vector as a representative embodiment, and it would be unnecessary to provide an explicit disclosure of other promoter sequences that achieve gene expression for purposes of nucleic acid immunization. Since the general flexibility of the approach was widely known, a disclosure of a representative promoter sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of promoter sequences that achieve gene expression for purposes of nucleic acid immunization. Additionally, the CMV expression vector is but a preferred embodiment. The state of the art of nucleic acid immunization indicated the inherent flexibility of the approach. The references incorporated by reference confirmed the state of the art. CMV was known not to be required to achieve immune responses. RSV is used in a human cancer vaccine. Even the CMV promoter itself exhibits flexibility in the sequences that can be used to achieve gene expression. The current state of the art of nucleic acid immunization celebrates the inherent flexibility of the approach a decade later. For these reasons, the rejection under 35 USC 112/1 is respectfully traversed.

1. <u>The CMV expression vector is but a preferred embodiment</u>

According to Specification at 6:1-18, "As referred to herein, the term 'encoding' is intended to mean that the subject nucleic acid may be transcribed by a cell, e.g., when the subject nucleic acid is linked to appropriate control sequences such as a promoter in a suitable vector (e.g., an expression vector) and the vector is introduced into a cell. ... Expression control sequences are known to those skilled in the art (see, e.g., Goeddel, Gene Expression Technology: Methods in

Enzymology 185, Academic Press, San Diego, CA (1990).[1] ... A preferred vector is the cytomegalovirus (CMV) expression vector which directs high levels of gene expression in muscle."

2. The state of the art indicated the inherent flexibility of the approach

Attached is Hasan et al. 1999 Journal of Immunological Methods 229: 1, which describes the state of the art of nucleic acid immunization at the time of the 23 Dec 1997 priority date. While published post-filing date, section 3.1.1 at page 7 on promoter selection and optimization describes the pre-filing date art (all the references were published 1997 or earlier). As can be seen from the review, viral promoters (CMV, RSV, and SV40) as well as mammalian house-keeping and tissue-specific promoters had been used to achieve gene expression.

3. The references incorporated by reference confirmed the state of the art

Specification at 17:4-16, citing references expressly incorporated by reference at 19:16, reiterates a description of the state of the art of nucleic acid immunization at the time of the 23 Dec 1997 priority date. Attached are copies of the references expressly incorporated by reference. The references confirmed the state of the art that viral promoters as well as other promoters had been used to achieve gene expression. Wolff et al. 1990 Science 247: 1465 (first report of "naked DNA," RSV); Ulmer et al. 1993 Science 259: 1745 (influenza, RSV or CMV); Raz et al. 1994 Proc. Natl. Acad. Sci. USA 91: 9519 (influenza, CMV or RSV); Doolan et al. 1996 J. Exp. Med. 183: 1739 (malaria, CMV); Sedegah et al. 1994 Proc. Natl. Acad. Sci. USA 91: 9866 (malaria, CMV); Tascon et al. 1996 Nature Med. 2: 888 (tuberculosis, CVM or promoter of a mammalian house-keeping gene); and Raz et al. 1993 Proc. Natl. Acad. Sci. USA 90: 4523 (immunological disease, RSV).

4. CMV was known not to be required to achieve immune responses

Although a CMV promoter-driven expression vector for an influenza virus nuclear protein stimulated higher specific antibody responses than did a vector with a Rous sarcoma virus (RSV) promoter in mice vaccinated by intradermal gene immunization, the vectors induced an equivalent immune response after intramuscular injection. Raz et al. 1994, supra. Thus, CMV was known not to be required to achieve immune responses that lead to protection.

5. RSV is used in a human cancer vaccine

HLA-B7/beta-2 microglobulin plasmid DNA/lipid complex, otherwise known as Allovectin-7, has been developed as a non-viral gene delivery product. Bergen et al. 2003 Expert

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[1] Attached.

Opin Biol Ther 3: 377, attached. Expression of both genes is driven by RSV promoter. Thus, RSV is used in a human cancer vaccine.

6. Even the CMV promoter itself exhibits flexibility in the sequences that can be used to achieve gene expression

The CMV promoter subsequently used in Amara et al. 2001 Science 292: 69 (n.9), attached, differs from the one in the example (Specification at 15:30 et seq.) in that it uses the CMV immediate early promoter *without* intron A.

7. The current state of the art celebrates the inherent flexibility of the approach a decade later

Attached is Muthumani et al. 2002 Vaccine 20: 1999, which describes the state of the art of nucleic acid immunization for HIV at the present time of 2002. As can be seen from the review, "[T]here has been little change to the original promoters ... in the last decade." At Abstract. While "DNA vaccination brings the full power of molecular biology to the development of the next generation of plasmid vaccines for HIV-1," the authors continue, "One of the central attractions of the DNA vaccine approach in general and for HIV vaccines in particular is the inherent flexibility of this approach." At p. 1999. col. 1, l. 1-5.

In sum, description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus (an expression vector) embraces. The CMV expression vector is but a preferred embodiment. The state of the art of nucleic acid immunization indicated the inherent flexibility of the approach. The references incorporated by reference confirmed the state of the art. CMV was known not to be required to achieve immune responses. RSV is used in a human cancer vaccine. Even the CMV promoter itself exhibits flexibility in the sequences that can be used to achieve gene expression. The current state of the art of nucleic acid immunization celebrates the inherent flexibility of the approach a decade later. For these reasons, the rejection under 35 USC 112/1 should be withdrawn.

CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 6/23/04

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IMMUNIZATION FOR EBOLA VIRUS INFECTION

Abstract

Ebola virus vaccines comprising nucleic acid molecules encoding Ebola viral proteins are provided. In one embodiment, the nucleic acid molecule encodes the transmembrane form of the viral glycoprotein (GP). In another embodiment, the nucleic acid molecule encodes the secreted form of the viral glycoprotein (sGP). In yet another embodiment, the nucleic acid molecule encodes the viral nucleoprotein (NP). Methods for immunizing a subject against disease caused by infection with Ebola virus are also provided.